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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/626,219	07/26/2000	Jeffrey Browning	A046 US	7978

7590 02/22/2002

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EXAMINER
YU, MISOOK

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 02/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/626,219	BROWNING ET AL.	
	Examiner	Art Unit	
	Misook Yu	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *11, 18,19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 12-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's election without traverse of Group 1 (claims 1-10 and 12-17) with species v (soluble LT beta receptor) in Paper No. 5 is acknowledged. Claims 11, 18, and 19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected claims, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 5.

Claims 1-10 and 12-17 are pending and examined on merits.

The substitute specification filed on 01/10/2002 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1-4, 7-10, 12-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "altering the humoral immune response" but it is not clear what are metes and bounds are for altering the humoral immune response. The specification at page 7, lines 1-3 refers humoral response as the immunological response of an animal to a foreign antigen whereby the animal produce antibodies to the foreign antigen. However, the specification is silent on what the metes and bounds are for "altering altering the humoral immune response". What does altering the humoral immune resposnse mean? Is it decreased or increased production of an antibody? If so how do you measure the humoral immune response?

Claim 1 recites "a)" but it is not clear what the metes and bounds for the "a)" is. Is there a missing b) of the method or it is a typo?

Claim 2 recites the limitation "said tumor". There is insufficient antecedent basis for this limitation in the claim.

Claim 3, 4, and 7-10 depend on the indefinite claim 2.

Claim 12, 13, 16, and 17 recites the limitation "said subject". There is insufficient antecedent basis for this limitation in the claim.

Claim 14 depends on the indefinite claim 13 and claim 15 depends on the indefinite claim 14.

For the purpose of this office action, the examiner will assume that any claim that recites "said tumor", and any claim that recites "said subject" mean that treatment of "said tumor" by administration of the instant invention to "said subject". However, this treatment does not relieve applicants of the burden of response to this rejection. See the second paragraph of the instant office action under first paragraph of 35 U.S.C. 112.

Claim 13 recites another TNF pathway but it is not clear what the metes and bounds are for another TNF pathway.

Claim 14 recites CD40/CD40 but it is not clear what the metes and bounds are for CD/CD?

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 and 12-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 1-10 and 12-17 are drawn to a method for altering the humoral immune response in an animal comprising administering a pharmaceutical composition which comprises ***a therapeutically effective amount*** of a lymphotoxin-beta receptor blocking agent. The specification discusses tumor treatment in detail, but it is not clear what disease is treated by altering the humoral immune response. Applicant's invention in the instant application is administering a pharmaceutical composition which comprises ***a therapeutically effective amount*** of a

lymphotoxin-beta receptor blocking agent for the humoral immune response in an animal. However, applicants admit, from page 18, last line through page19, lines 1-8, that they have not established the therapeutically effective amount of lymphotoxin-beta receptor blocking agent for the purpose stated in the preamble, stating that "the general dosage is established by preclinical and clinical trials, which involve extensive experiments to determine the beneficial and deleterious effects on the patient of different dosages of the compound."

The specification in Table 1 shows that the LN weight of the sacrificed mice, a species of claim 5, that received the lymphotoxin-beta receptor blocking agent, is lower compare to the control. However, the data in Table 1 does not establish ***a therapeutically effective amount*** of the lymphotoxin-beta receptor blocking agent. The specification fails to establish that: (1) ***a therapeutically effective amount*** of a lymphotoxin-beta receptor blocking agent for follicular lymphoma in claim 2 (2) ***a therapeutically effective amount*** of a lymphotoxin-beta receptor blocking agent for a mammal in claim 5, a human in claim 6, (3) any evidence exists for claims 10-17. An effective therapeutic protocol for the treatment or prevention of the formation of a tumor is subject to a number of factors which enter the picture beyond the LT pathway. See the entire abstract of Hillion et al. Demonstrating the smaller LN weight cannot alone support the predictability of the method for treating said tumor through administration of lymphotoxin-beta receptor blocking agent. Tumor growth is a complex and multiple step process that proceeds by the acquisition of successive genetic insults (Hagemeijer, Leukemia, 1992, Vol. 6, Suppl. 4, pp. 16-18). The establishment and growth of a tumor is subject to variables beyond the single signaling pathway. The ability of a host to suppress and thereby prevent the tumor from establishing itself will vary depending upon factors such as the condition of the host, the type and stage of tumor. The specification has not given instruction for the dose regiment to be used, nor the mode of delivery in vivo, in order to effectively target the claimed tumor cells. Compare the mode of delivery in Table 1 vs. routes of administration cited at page 18. Applicant fails to show the reason why the more convenient oral route is not used for the delivery of the lymphotoxin-beta receptor blocking agent. Because of the limited

guidance, lack of working examples, and unpredictability of success for pharmaceutical treatments using the lymphotoxin-beta receptor blocking agent, it is concluded that undue experimentation would be required to use the invention as claimed.

Furthermore, claim 1 is broadly drawn to a method using any "blocking agent", but the specification only discloses only a soluble LT-beta receptor and various anti-LT-beta receptor antibodies. Considering limited guidance, and unpredictability of success for pharmaceutical treatments using the lymphotoxin-beta receptor blocking agent, it is concluded that undue experimentation would be required to make the full scope of blocking agents.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Misook Yu whose telephone number is 703-308-2454. The examiner can normally be reached on 8 A.M. to 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Misook Yu
February 4, 2002

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1800
1600